

What is claimed is:

1. A context-activated protide comprising an amino acid sequence selected from the group consisting of SEQ ID
5 NOS: 1, 2, 3 and 4.

2. A context-activated protide consisting of the amino acid sequence selected from the group consisting of
SEQ ID NOS: 1, 2, 3 and 4.
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3. A context-activated protide comprising at least one activator site and two or more effectors, wherein at least two of said effectors have distinct biological functions.
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4. The protide of claim 3, wherein said activator site is context-activated.

5. The protide of claim 4, wherein said context-
20 activation initiates said biological functions of said effectors.

6. The protide of claim 4, wherein said context-activation results from a physiological condition.
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7. The protide of claim 6, wherein said physiological condition is selected from the group consisting of acidity, alkalinity, ionic strength and osmotic strength.

8. The protide of claim 4, wherein said context-activation results from association with an activator molecule.

5 9. The protide of claim 8, wherein said activator molecule modifies said activator site upon association.

10 10. The protide of claim 9, wherein said modification comprises cleavage of said activator site.

11. The protide of claim 10, wherein said activator molecule is an enzyme.

12. The protide of claim 11, wherein said activator molecule is selected from the group consisting of
15 protease, esterase and lipase.

13. The protide of claim 12, wherein said activator molecule is a protease.

20 14. The protide of claim 13, wherein said activator is expressed by a bacterial pathogen.

15. The protide of claim 14, wherein said activator
25 molecule is a surface protein transpeptidase (sortase).

16. The protide of claim 15, wherein said bacterial pathogen is *Staphylococcus aureus*.

30 17. The protide of claim 13, wherein said activator molecule is a serine protease.

18. The protide of claim 13, wherein said activator is present in the context of vascular injury.

19. The protide of claim 18, wherein said protease
5 is a clotting cascade protease.

20. The protide of claims 17 or 19, wherein said protease is thrombin.

10 21. The protide of claim 13, wherein said protease is a complement fixing protease.

22. The protide of claim 21, wherein said complement fixing protease is a C3 convertase.
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23. The protide of claim 22, wherein said C3 convertase is selected from the group consisting of C4b2A and C3bBb.

20 24. The protide of claim 21, wherein said complement fixing protease is a C5 convertase.

25 25. The protide of claim 13, wherein said activator is present in the context of tumor cells.

26. The protide of claim 25, wherein said activator is a tumor-specific protease.

27. The protide of claim 26, wherein said tumor-
30 specific protease is matrix bound.

28. The protide of claim 27, wherein said tumor-specific protease is a matrix metalloproteinase.

29. The protide of claim 13, wherein said activator
5 is present in the context of an inflammatory response.

30. The protide of claim 30, wherein said activator activates a cytokine effector.

10 31. The protide of claim 31, wherein said effector is Interleukin-8.

32. The protide of claim 31, wherein said effector is a chemotactic cytokine (chemokine).
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33. The protide of claim 13, wherein said activator is a peptide selected from the group consisting of thrombin, bradykinin, elastase and metalloproteinase.

20 34. The protide of claim 3, wherein said distinct biological functions are selected from the group consisting of antimicrobial, immunomodulatory, tumoricidal, pro-apoptotic, anti-apoptotic, pro-angiogenic, anti-angiogenic and hemolytic.

25 35. The protide of claim 3, wherein said effectors comprise a peptide.

36. The protide of claim 3, wherein said effectors
30 comprise a non-peptide.

37. The protide of claim 3, wherein one of said biological functions is immunomodulatory.

38. The protide of claim 3, wherein one of said
5 biological functions is antimicrobial.

39. The protide of claim 3, wherein one of said biological functions is tumoricidal.

10 40. The protide of claim 3, wherein one of said biological functions is pro-apoptotic.

41. The protide of claim 3, wherein one of said biological functions is anti-apoptotic.
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42. The protide of claim 3, wherein one of said biological functions is anti-angiogenic.

43. The protide of claim 3, wherein one of said
20 biological functions is fungicidal.

44. The protide of claim 3, wherein one of said biological functions is virucidal.

25 45. The protide of claim 3, wherein one of said biological functions is hemolytic.

46. The protide of claim 3, wherein said context-activated protide has two effectors.

47. The protide of claim 3, wherein said distinct biological functions of said effectors comprise antimicrobial and immunomodulatory.
- 5 48. The protide of claim 35, wherein said peptide belongs to a family selected from the group consisting of defensins, cecropins, cryptidins, magainins, protegrins, indolicidins, HIV viral protein R (Vpr), tissue factors, mellittins, and/or bacteriocidins.
- 10 49. A context-activated protide comprising one activator site and two effector peptides having distinct biological functions, wherein said distinct biological functions are antimicrobial and immunomodulatory.
- 15 50. The context-activated protide of claim 3 or 49, wherein said context-activation initiates said biological functions of said effectors.
- 20 51. The context-activated protide of claim 50, wherein said context-activation results from the association between an enzyme expressed by a bacterial pathogen with said activator site.
- 25 52. The context-activated protide of claim 51, wherein said bacterial pathogen is *S. aureus*.
- 30 53. The context-activated protide of claim 51, wherein said *S. aureus* belongs to a methicillin-resistant strain.

54. The context-activated protide of claim 52, wherein said *S. aureus* is selected from the group consisting of a vancomycin-resistant strain and intermediate-resistant to vancomycin strain.

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55. The context-activated protide of claim 52, wherein said enzyme is a surface protein transpeptidase (sortase).

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56. The context-activated protide of claim 3 or 49, wherein said protide is cleaved upon activation into separate effector domains, wherein one of said effector domains has said antimicrobial function, and wherein said second effector domain has said immunomodulatory function.

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57. The protide of claim 56, wherein said antimicrobial function comprises directly killing said bacterial pathogen.

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58. The protide of claim 56, wherein said antimicrobial function comprises inhibition of said surface protein transpeptidase (sortase).

59. The protide of claim 49, wherein one of said effector peptides comprises interleukin-8, and wherein said other effector peptide comprises Defensin hNP-1, and wherein said activator comprises a protease.

60. The protide of claim 59, wherein said protease is a clotting cascade protease.

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61. The protide of claim 59, wherein said protease is thrombin.

62. The protide of claim 59, wherein said protease
5 is a complement fixing protease.

63. The protide of claim 62, wherein said complement fixing protease is a C3 convertase.

10 64. The protide of claim 63, wherein said C3 convertase is selected from the group consisting of C4b2A and C3bBb.

65. The protide of claim 62, wherein said complement
15 fixing protease is a C5 convertase.

66. A context-activated protide comprising one activator site and two effector peptides having distinct biological functions, wherein said distinct biological
20 functions are anti-toxic and antimicrobial.

67. A context-activated protide comprising one activator site and two effector peptides having distinct biological functions, wherein said distinct biological
25 functions are anti-angiogenic and antimicrobial.

68. A context-activated protide comprising one activator site and two effector peptides having distinct biological functions, wherein said distinct biological
30 functions are pro-apoptotic and anti-angiogenic.

5 69. A method of treating vascular injury, said method comprising administering to a subject a therapeutically effective amount of the context-activated protide of claim 56.

 70. A method of treating a neoplastic
10 condition, said method comprising administering to a subject a therapeutically effective amount of the protide of claim 68.

 71. A method of treating a microbial
infection, said method comprising administering to a
15 subject a therapeutically effective amount of the protide of claim 66.

 72. A method of treating a condition
associated with decreased cell death, said method
comprising administering to a subject a therapeutically
20 effective amount of the protide of claim 68.

 73. A method of treating an inflammatory
condition, said method comprising administering to a
subject a therapeutically effective amount of the protide
of claim 1 or 2.